

(FILE 'HOME' ENTERED AT 14:44:52 ON 16 MAY 2003)

FILE 'CAPLUS' ENTERED AT 14:45:19 ON 16 MAY 2003

L1 421 S (VIRTUAL OR (IN SILICO)) (3W) SCREEN?  
L2 179 S L1 AND LIBRARY  
L3 11 S L2 AND FRAGMENT  
L4 12 S L2 AND FRAGMENT?

=> d bib,abs 4,6,8

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS  
AN 2002:451675 CAPLUS  
DN 137:345419  
TI **Fragment** analysis in small molecule discovery  
AU Merlot, Cedric; Domine, Daniel; Church, Dennis J.  
CS Scientific Computing Department, Serono Pharmaceutical Research Institute,  
Geneva, Switz.  
SO Current Opinion in Drug Discovery & Development (2002), 5(3), 391-399  
CODEN: CODDDFF; ISSN: 1367-6733  
PB PharmaPress Ltd.  
DT Journal; General Review  
LA English  
AB A review. Cheminformatics is playing an ever-increasing role in small  
mol. drug discovery. The widespread use of high-throughput screening  
(HTS) and combinatorial chem. techniques has led to the generation of  
large amts. of pharmacol. data which, in turn, has catalyzed the  
development of computational methods designed to reduce the time and cost  
in identifying mols. suitable for pharmaceutical development. This review  
focuses on recent advances in the field of substructure anal., an  
increasingly popular data mining technique with applications at many  
levels of the discovery process, including HTS, compd. **library**  
design, **virtual screening**, and the prediction of biol.  
activity.

RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:199843 CAPLUS  
TI **Virtual** high-throughput **screening** of large datasets  
using TAE/RECON descriptors  
AU Sukumar, Nagamani; Breneman, Curt M.; Katt, William P.  
CS Department of Chemistry, Rensselaer Polytechnic Institute, Troy, NY,  
12180, USA  
SO Abstracts of Papers - American Chemical Society (2001), 221st, COMP-057  
CODEN: ACSRAL; ISSN: 0065-7727  
PB American Chemical Society  
DT Journal; Meeting Abstract  
LA English  
AB Recent developments using the method of Transferable Atom Equiv. (TAE)  
reconstruction will be discussed, including Wavelet Coeff. Descriptors  
(WCDs) and the evolution of automated atom type generation tools and  
automated lead testing algorithms. The TAE method, based on the Theory of  
Atoms in Mols., is an algorithm for the rapid reconstruction of mol.  
charge densities and charge-d.-based electronic properties of mols. using  
at. charge d. **fragments** precomputed from ab initio  
wavefunctions. The RECON algorithm inputs mol. geometries for a single  
mol. or an entire pharmaceutical database, dets. atom types and  
environments, assigns the closest match from a **library** of atom  
types, and combines the densities of the at. **fragments** to  
compute a large set of new and traditional QSAR descriptors. The TAE  
**library** contains information describing topol. features of the at.  
charge d. and at. charge d.-based descriptors, allowing for rapid  
retrieval of the **fragments** and mol. assembly. QSPR and QSER

indexes for individual proteins or large databases can be computed within seconds. We expect this emerging technol. to become a valuable tool in the rational design of target mols. having specific desired properties.

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS  
AN 2000:807156 CAPLUS  
DN 134:95130  
TI Development and screening of a polyketide virtual **library** for  
drug leads against a motilide pharmacophore  
AU Siani, M. A.; Skillman, A. G.; Carreras, C. W.; Ashley, G.; Kuntz, I. D.;  
Santi, D. V.  
CS Kosan Biosciences, Hayward, CA, USA  
SO Journal of Molecular Graphics & Modelling (2000), 18(4/5), 497-511  
CODEN: JMGMFI; ISSN: 1093-3263  
PB Elsevier Science Inc.  
DT Journal  
LA English  
AB A virtual **library** of macrocyclic polyketide mols. was generated  
and screened to identify novel, conformationally constrained potential  
motilin receptor agonists ("motilides"). A motilide pharmacophore model  
was generated from the potent 6,9-enol ether erythromycin and known  
derivs. from the literature. The pharmacophore for each mol. conformation  
was a point in a distance-vol. space based on presentation of the putative  
binding moieties. Two methods, one **fragment** based method and  
the other reaction based, were explored for constructing the polyketide  
virtual **library**. First, a virtual **library** was  
assembled from monomeric **fragments** using the CHORTLES language.  
Second, the virtual **library** was assembled by the in silico  
application of all possible polyketide synthase enzyme reactions to  
generate the product **library**. Each **library** was  
converted to low-energy 3D conformations by distance geometry and std.  
minimization methods. The distance-vol. metric was calcd. for low-energy  
conformations of the members of the **virtual** polyketide  
**library** and **screened** against the enol ether  
pharmacophore. The goal was to identify novel macrocycles that satisfy  
the pharmacophore. We identified three conformationally constrained,  
novel polyketide series that have low-energy conformations satisfying the  
distance-vol. constraints of the motilide pharmacophore.  
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT